REMARKS

Rejection under 35 USC §102(b)

Claims 1, 4-7, 10-14 and 17-19 have been rejected under 35 USC §102(b) as being anticipated by Ferguson, US Patent No. 5,520,926. It is the Examiner's position that the teaching in Ferguson of the use of mannose -6- and 1-phosphates to treat fibrotic disorders anticipates the present claims relating to the use of the same material to exfoliate skin, to stimulate the production of glycosaminoglycans in skin, and to treat conditions associated with reduced levels of glycosaminoglycans, such as skin aging (chrono- or photo-), wrinkles and the like. The rejection, stated as follows, is repeated from the previous office action of August 29, 2005 (rejecting claims 7, 10-14 and 17-19):

> "Applicants claim method for increasing levels of glycosaminoglycans in skin comprising applying to the skin a composition containing an effective amount of a mannose phosphate. Additional limitations in the dependent claims include the mannose phosphate being mannose-6-phosphate, the use of a specific amount of mannose phosphate, and the method having specific skin conditions, which include dry skin, lines and wrinkles, and symptoms of chrono-and photoaging.
>
> The Ferguson patent discloses mannose 6- and 1-phosphates as being useful in the treatment of fibrotic disorders (see abstract). See column 4, lines 28-31, wherein the Ferguson patent discloses the invention thereof as being 'primarily of interest in relation to skin wounds, whether arising through surgery or other wise, including severe abrasions laceration and burns, but is also applicable to fibrotic disorders, which includes photo-damage.' See the examples disclosed in the Ferguson patent wherein the amounts of mannose phosphates used in the treatments are disclosed, which appear to be within the scope of the amounts of mannose phosphate set forth in the instant claims. The use of mannose phosphate to treat fibrotic disorders, which include and photo-damage, in the Ferguson patent anticipates the instantly claimed method of increasing levels of glycosaminoglycans in skin, since the instant claims disclose that photoaging of skin is a condition associated with reduced level of glycosaminoglycans in the skin (see instant Claim 14)."

The Examiner states further, in the present office action:

> ""The method of exfoliating skin comprising applying to the skin a composition comprising mannose phosphate and the application of mannose phosphate for the treatment of photoaging skin are based on the same principle that involves removing the outmost layer of skin and replacing the outer layer with newly generated skin cells. Hence, upon further consideration, the subject of Claims 1 and 4-6 is inherently identical to the method of Claims 13 and 14 since the same mechanism

used to carry out the subject matter of Claims 1 and 4-6 is identical to the mechanism used in Claims 13 and 14.

Also Applicants argument hat there is a difference between the photo-damage skin of the Ferguson patent and the photo-aged skin of the instant claims is not persuasive. Hence Applicants arguments from a legal point of view is not persuasive.

The mannose 6-phosphate applied to skin disclosed in the instant claims is identical to the mannose 6-phosphate applied to skin disclosed in the Ferguson patent. Applicants are reminded that products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present. *In re Spada* 15 USPQ 2d 1655, 1658 (Fed. Cir. 1990). See MPEP 21112.01."

Claim 14 has been amended to make it clear that the conditions associated with reduced levels of glycosaminoglycans, including dry skin, lines and wrinkles are examples of the symptoms of chrono- and photo-aging. The amendment is consistent with the disclosure in the present specification at page 5, lines 2-5. The significance of the amendment will be addressed more specifically below.

The Examiner's position regarding "photo-aging" as the term is used in the art generally, and in the present specification specifically, and "photodamage" as it relates to the Ferguson reference, is simply incorrect, both technically and legally.

To address the technical error first, equating photoaging with photodamage as these terms are used in the present specification and in the Ferguson reference, respectively, is based on a misreading of each of the present specification and the reference. Ferguson states, in column 4, lines 28-33,

> "Although the invention is primarily of interest in relation to skin wounds, whether arising through surgery or otherwise, including severe abrasions lacerations and burns, it is also applicable to fibrotic skin disorders, e.g. *photo-damage (which is believed to up-regulate certain effectors of an increase in fibrous tissue)*...[emphasis added]".

The fibrotic disorders referred to in Ferguson are characterized by an excess of fibrous material in the skin. An exemplary list of fibrotic diseases is found in column 1, lines 33-37 in the reference. Unlike the photo-damage disclosed in the reference, the present specification refers to photo-aging, which includes the symptoms of dry skin, lines and wrinkles. Claim 14 as amended

makes it clear that the aforementioned symptoms are characteristic of photo-aging and not separate conditions therefrom. In fact, it is well-known to those skilled in the cosmetic arts as well as in photochemistry and photobiology, that "solar UV radiation damages human skin, affecting skin tone and resiliency, and leading to premature aging (i.e. photo-aging), the symptoms of which include leathery texture, wrinkles, mottled pigmentation, laxity and sallowness", as stated in the attached abstract "Molecular mechanisms of photoaging in human skin in vivo and their prevention by all-trans retinoic acid", published in 1999. As indicated in the abstract, it has been proposed that photo-aging results from UV induction of enzymes which degrade skin collagen (i.e. fibrous material which keeps skin from sagging).

Since photodamage, as defined in Ferguson, and photo-aging, as used in the present specification are mutually exclusive conditions, then, strictly from a technical point of view, there is no anticipation of the present claims by the Ferguson reference.

Moreover, the Applicants cannot agree with the Examiner's reasoning for withdrawing the allowability of claims 1 and 4-6, drawn to a method of exfoliating the skin. The Examiner contends that if claims 7, 10-14, and 17-19 are not allowable for the reasons given, then claims 1 and 4-6 also are not allowable because the methods are inherently the same as the method of claims 7, 10-14, and 17-19. Nevertheless, the Applicants are not claiming a method of applying a mannose phosphate to the skin. The Applicants are claiming, in claim 1, a method of exfoliating the skin which supplements the natural sloughing process, and smoothes the surface texture of the skin, as measured by a reduction in flakiness. On the other hand, claim 13 is directed to a method of treating a skin condition associated with a reduced level of glycosaminoglycans in the skin. The enhanced synthesis of glycosaminoglycans results in increased water retention in the skin and skin plumping with a reduction in the appearance of lines and wrinkles. The respective populations of users of the two methods are not necessarily the same. The population of users having flakey skin in need of exfoliation will not necessarily be that population having dry, and/or wrinkled skin associated with aging. Young skin may also exhibit flakiness, and dry skin,

resulting from photo-aging, may not necessarily be flakey. Furthermore, the population of users having photo-aged skin, and who are desirous of obtaining plumped skin which will reduce the appearance of dryness, lines and wrinkles, and sagging of the skin, will also not necessarily be the same population merely in need of exfoliation for treating flakey skin.

Similarly, from a legal point of view, the basis for rejection of the claims on the ground of anticipation also fails. Absence of a claim element from a prior art reference negates anticipation. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 224 USPQ 409 (Fed. Cir. 1984). The Applicants remind the Examiner that a composition comprising a mannose phosphate is not being claimed, and therefore *In re Spada* and MPEP 2112.01 have been misapplied to the present claims. The Applicants are instead claiming three methods: a method of exfoliating skin, a method for increasing levels of glycosaminoglycans in skin, and a method of treating a skin condition associated with a reduced level of glycosaminoglycans in the skin. The reference fails to disclose a method of exfoliating skin, a method for increasing levels of glycosaminoglycans in skin and a method of treating a skin condition associated with a reduced level of glycosaminoglycans in the skin. Since Ferguson fails to disclose each and every element of the claimed inventions, there is no anticipation of the present claims by the reference.

Should the Examiner's basis of rejection be anticipation based on inherency, then this also fails. For the concept of inherency to apply in an anticipation rejection, the subject matter being claimed must undeniably and irrefutably flow from the prior art disclosure. *Hughes aircraft Co. v. United States*, 8 USPQ 2d 1580 (Ct. Cl. 1988). Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstance is not sufficient. *In re Oelrich and Divigard*, 212 USPQ 323 (CCPA) 1981). The skin to which a mannose phosphate would be applied according to the Ferguson patent (skin exhibiting wounds or fibrotic disorders) is clearly not the same skin to which a mannose phosphate would be applied according to the methods of the present invention (flakey skin in need of exfoliation, or dry and/or wrinkled skin associated with aging). Therefore, the

result claimed in the present application would not "irrefutably flow" from the disclosure of Ferguson. Because the present invention addresses application of the mannose phosphate to a type of skin different from that disclosed in Ferguson, there can be no anticipation of the present claims by Ferguson. See *Perricone v. Medicis Pharmaceutical Corporation*, slip op. (CAFC, 05-1022-1023, December 2005).

In view of the technical and legal arguments presented above, it is clear that the rejection of claims 1, 4-7, 10-14 and 17-19 as anticipated by Ferguson is improper and should be withdrawn.

Conclusion

In view of the arguments presented above, it is believed that independent claims 1, 7 and 13, and the claims dependent therefrom, are patentable over the reference. With the submission of claims and amendments herein, the application is in condition for allowance, and the issuance of a Notice of Allowance is therefore respectfully solicited. The Examiner is encouraged to contact the undersigned by telephone if it is believed that discussion will resolve any outstanding issues.

A petition and fee for extension of time for two months, and a Notice of Appeal and the requisite fee are being submitted concurrently with this response.

Date: 9/18/06

Respectfully submitted,

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Molecular mechanisms of photoaging in human skin in vivo and their prevention by all-trans retinoic acid

Photochemistry and Photobiology, Feb 1999 by Fisher, Gary J, Talwar, Harvinder S, Lin, Jiayuh, Voorhees, John J

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ABSTRACT

Solar UV radiation damages human skin, affecting skin tone and resiliency and leading to premature aging (photoaging), the symptoms of which include leathery texture, wrinkles, mottled pigmentation, laxity and sallowness. We propose that photoaging results largely from UV induction of matrix metalloproteinases (MMP) that degrade skin collagen. We find that pretreatment of human skin with all-trans retinoic acid (tRA) inhibits UV induction of MMP, suggesting that tRA can protect against UV-induced collagen destruction and may therefore be able to lessen the effects of photoaging. The tRA prevents UV-induced accumulation of c-Jun protein, which is required for MMP gene expression. Activation of c-Jun transcriptional activity requires N-terminal phosphorylation. The majority of c-Jun in human skin in vivo is Nterminal phosphorylated. Topically applied tRA does not inhibit N-terminal phosphorylation by UV-induced c-Jun kinase activity in human skin. The tRA likely acts to reduce UV induction of c-Jun protein by stimulating its breakdown through the ubiquitin-proteasome pathway.